

What is claimed is:

1. A method of treating a mammal suffering from or susceptible to stroke, brain or spinal cord injury or ischemia, or heart attack, comprising administering to the mammal a therapeutically effective amount of a neuregulin, or fragment or derivative of a neuregulin, or a nucleic acid encoding a neuregulin or a fragment or derivative of a neuregulin.

2. A method of treating a mammal suffering from or susceptible to optic nerve injury or retinal injury or ischemia, comprising administering to the mammal a therapeutically effective amount of a neuregulin, or fragment or derivative of a neuregulin, or a nucleic acid encoding a neuregulin or a fragment or derivative of a neuregulin.

3. A method of treating a mammal suffering from or susceptible to effects of post-surgical neurological deficits, hypoxia or hypoglycemia, comprising administering to the mammal a therapeutically effective amount of a neuregulin, or fragment or derivative of a neuregulin, or a nucleic acid encoding a neuregulin or a fragment or derivative of a neuregulin.

4. A method of treating a mammal suffering from or susceptible to epilepsy, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, Alzheimer's disease, Down's Syndrome, Korsakoff's disease, or age-dependent dementia, comprising administering to the mammal a therapeutically effective amount of a neuregulin, or fragment or derivative of a neuregulin, or a nucleic acid encoding a neuregulin or a fragment or derivative of a neuregulin.

5. The method of claim 1 wherein the neuregulin, or fragment or derivative of a neuregulin, or a nucleic acid encoding a neuregulin or a fragment or derivative of a neuregulin is administered after the subject has suffered a stroke, brain or spinal cord injury or ischemia, or heart attack.

6. The method of claim 5 wherein the neuregulin, or fragment or derivative of a neuregulin, or a nucleic acid encoding a neuregulin or a fragment or derivative of a neuregulin is administered to the subject for at least about two weeks after the subject has suffered a stroke, brain or spinal cord injury or ischemia, or heart attack.

~~7. A method of any one of claims 1-6 wherein a neuregulin or a fragment or derivative thereof is administered to the mammal.~~

8 A method of claim 7 wherein the neuregulin or fragment or derivative thereof comprises an amino acid sequence of the following formula:

WYBAZCX

wherein WYBAZCX is composed of amino acid sequences that include one or more sequences shown in FIGS. 1 through 15 (which includes SEQ ID NOS:2, 4, 5, 8, 9, 12, 14, 15, 18, 19, 22, 23, 26, 27, 30, 33, 35, 38, 39, 41, 44, 45 and 48), wherein W comprises the polypeptide segment F, or is absent; wherein Y comprises the polypeptide segment E, or is absent; wherein Z comprises the polypeptide segment G or is absent; and wherein X comprise a polypeptide segment selected from the group consisting of C/D HKL, C/D H, C/D HL, C/D D, C/D' HL, C/D' HKL, C/D' H, C/D' D, C/D C/D' HKL, C/D C/D' H, C/D C/D' HL, C/D C/D' D, C/d D'H, C/D D' HL, C/D D' HKL, C/D' D' H, C/D' D' HL, C/D' D' HKL, C/D C/D' D' H, C/D C/D' D' HL and C/D C/D' D' HKL, and preferably that either

- a) at least one of F, Y, B, A, Z, C or X is of bovine origin; or
- b) Y comprises the polypeptide segment E; or
- c) X comprises the polypeptide segments C/D HKL, C/D D, C/D' HKL, C/D C/D' HKL, C/D C/D' D, C/D D' H, C/D D' HL, C/D D' HKL, C/D' D' H, C/D' D' HKL, C/D C/D' D'H, C/D C/D' D HL, C/D C/D' D' HKL, C/D'H, C/D C/D' H or C/D C/D' HL.

~~9~~ The method of claim 7 wherein the neuregulin or fragment or derivative thereof a) has at least one of F, Y, B, A, Z, C or X is of bovine origin; or b) Y comprises the polypeptide segment E; or c) X comprises the polypeptide segments C/D HKL, C/D D, C/D' HKL, C/D C/D' HKL, C/D C/D' D, C/D D H, C/D D' HL, C/D D' HKL, C/D C/D' D' H, C/D C/D' D HL, C/D C/D' D' HKL, C/D' H, C/D C/D' H or C/D C/D' HL.

10. The method of claim 7 wherein the neuregulin or fragment or derivative thereof comprises FBA polypeptide segments, FEBA polypeptides segments, EBA polypeptide segments, EBA' polypeptide segments or FEBA' polypeptide segments.

Rule a

1. *What is the purpose of the study?*
 2. *What are the research objectives?*
 3. *What is the research design?*
 4. *What are the variables?*
 5. *What is the sample size?*
 6. *What are the data sources?*
 7. *What are the data collection methods?*
 8. *What are the data analysis methods?*
 9. *What are the results?*
 10. *What are the conclusions?*
 11. *What are the limitations?*
 12. *What are the recommendations?*

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11. A method of claim 7 wherein the neuregulin is encoded by a nucleic acid that comprises one of SEQ ID NOS:49, 51 and 53.
12. A method of claim 7 wherein the neuregulin or fragment or derivative thereof is encoded by a nucleic acid that comprises a sequence that has at least about 70% sequence identity to one of SEQ ID NOS:49, 51 and 53.
13. A method of claim 7 wherein the neuregulin or fragment or derivative thereof is encoded by a sequence that hybridizes to one of SEQ ID NOS:49, 51 or 53 under normal stringency conditions.
14. A method of claim 7 wherein the neuregulin or fragment or derivative thereof is encoded by a sequence that hybridizes to one of SEQ ID NOS:49, 51 or 53 under high stringency conditions.
15. A method of claim 7 wherein the neuregulin or fragment or derivative has at least about 70% sequence identity to SEQ ID NOS:50, 52 or 54.
16. A method of claim 7 wherein the neuregulin or fragment or derivative thereof is encoded by a nucleic acid that comprises a sequence that has at least about 70% sequence identity to one of SEQ ID NO:20 (Figure 7); SEQ ID NO:21 (Figure 7); SEQ ID NO:24 (Figure 8); SEQ ID NO:25 (Figure 8); SEQ ID NO:28 (Figure 9); or SEQ ID NO:29 (Figure 9).
17. A method of claim 7 wherein the neuregulin or fragment or derivative thereof is encoded by a sequence that hybridizes to one of SEQ ID NO:20 (Figure 7); SEQ ID NO:21 (Figure 7); SEQ ID NO:24 (Figure 8); SEQ ID NO:25 (Figure 8); SEQ ID NO:28 (Figure 9); or SEQ ID NO:29 (Figure 9) under normal stringency conditions.
18. A method of claim 7 wherein the neuregulin or fragment or derivative comprises a sequence that has at least about 70% sequence identity to any of the peptide sequences shown in Figures 7, 8 or 9 of the drawings.
19. A method of claim 7 where the neuregulin or fragment or derivative comprises a sequence that has at least about 80 percent homology to any of the peptide sequences shown in Figures 7, 8 or 9.
20. A method of claim 7 where the neuregulin or fragment or derivative comprises a sequence that has at least about 90 percent homology to any of the peptide sequences shown in Figures 7, 8 or 9.

~~21. A method of claim 7 wherein the neuregulin or fragment or derivative comprises a sequence that has at least about 95 percent homology to any of the peptide sequences shown in Figures 7, 8 or 9.~~

22. A method of claim 7 wherein the neuregulin or fragment or derivative comprises a sequence that is shown in Figures 7, 8 or 9.

23. A method of any one of claims 1-6 wherein a nucleic acid encoding a neuregulin or a fragment or derivative thereof is administered to the mammal.

24. A method of claim 23 wherein the nucleic acid is SEQ ID NO:49, 51 or 53, or the complement thereof.

25. A method of claim 23 wherein the nucleic or fragment or derivative thereof encodes a neuregulin or neuregulin fragment or derivative that comprises an amino acid sequence of the following formula:

WYBAZCX

wherein WYBAZCX is composed of amino acid sequences that include one or more sequences shown in FIGS. 1 through 15 (which includes SEQ ID NOS:2, 4, 5, 8, 9, 12, 14, 15, 18, 19, 22, 23, 26, 27, 30, 33, 35, 38, 39, 41, 44, 45 and 48), wherein W comprises the polypeptide segment F, or is absent, wherein Y comprises the polypeptide segment E, or is absent; wherein Z comprises the polypeptide segment G or is absent; and wherein X comprise a polypeptide segment selected from the group consisting of C/D HKL, C/D H, C/D HL, C/D D, C/D' HL, C/D' HKL, C/D' H, C/D' D, C/D C/D' HKL, C/D C/D' H, C/D C/D' HL, C/D C/D' D, C/D D' HL, C/D D' HKL, C/D' D' H, C/D' D' HL, C/D' D' HKL, C/D C/D' D' H, C/D C/D' D' HL and C/D C/D' D' HKL.

26. The method of claim 25 wherein the neuregulin or neuregulin fragment or derivative a) has at least one of F, Y, B, A, Z, C or X is of bovine origin; or b) Y comprises the polypeptide segment E; or c) X comprises the polypeptide segments C/D HKL, C/D D, C/D' HKL, C/D C/D' HKL, C/D C/D' D, C/D D H, C/D D' HL, C/D D' HKL, C/D C/D' D' H, C/D C/D' D HL, C/D C/D' D' HKL, C/D' H, C/D C/D' H or C/D C/D' HL.

27. The method of claim 25 wherein the neuregulin or neuregulin fragment or derivative comprises FBA polypeptide segments, FEBA polypeptides segments,

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EBA polypeptide segments, EBA' polypeptide segments or FEBA' polypeptide segments.

28. A method of claim 23 wherein the nucleic acid comprises a sequence that hybridizes to SEQ ID NO:20 (Figure 7); SEQ ID NO:21 (Figure 7); SEQ ID NO:24 (Figure 8); SEQ ID NO:25 (Figure 8); SEQ ID NO:28 (Figure 9); or SEQ ID NO:29 (Figure 9) under normal stringency conditions.

29. A method of claim 23 wherein the nucleic acid comprises a sequence that hybridizes to SEQ ID NO:20 (Figure 7); SEQ ID NO:21 (Figure 7); SEQ ID NO:24 (Figure 8); SEQ ID NO:25 (Figure 8); SEQ ID NO:28 (Figure 9); or SEQ ID NO:29 (Figure 9) under high stringency conditions.

30. A method of claim 23 wherein the nucleic acid comprises a sequence that has at least about 70 percent homology to any of the nucleic acid sequences shown in Figures 7, 8 or 9.

31. A method of claim 23 wherein the nucleic acid comprises a sequence that has at least about 80 percent homology to any of the nucleic acid sequences shown in Figures 7, 8 or 9.

32. A method of claim 23 wherein the nucleic acid comprises a sequence that has at least about 90 percent homology to any of the nucleic acid sequences shown in Figures 7, 8 or 9.

33. A method of claim 23 wherein the nucleic acid comprises a sequence that has at least about 95 percent homology to any of the nucleic acid sequences shown in Figures 7, 8 or 9.

34. A method of claim 23 wherein the nucleic acid comprises a sequence shown in Figures 7, 8 or 9.

35. A method of any one of claims 1-34 wherein the administered neuregulin fragment or derivative, or the administered nucleic acid encodes a neuregulin fragment or derivative exhibits at least about a 10% reduction in infarct volume in an *in vivo* cerebral ischemia assay.

36. A method of any one of claims 1-35 wherein the mammal is a human.

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